REMARKS

Applicants respectfully request entry of amendments to claims 1, 3, 8, 9, 13, 25, and 36. Claims 2, 10, 11, 14-22, 24, 27-35, 37, 39-47, and 49-79 were previously canceled. Support for the amendments can be found throughout the specification, including paragraph [0013], Figure 5, and the originally filed claims and, therefore, do not add new matter.

Applicants submit that pending claims 1, 3-9, 12, 13, 23, 25, 26, 36, 38, 48, 80, and 81 are in condition for allowance, and respectfully request that the claims as amended be entered.

Rejection Under 35 U.S.C. §112, Second Paragraph

Claims 1, 3-9, 12-13, 23, 25, 26, 36, 38, 48, 80, and 81 stand rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite.

Applicants traverse the rejection as it might apply to amended claims, including claims dependent therefrom, for the reasons given below.

The Office Action alleges that the term "specific detection" is unclear. Further, it is alleged that it is unclear as to how detecting non-consensus regions which are specific to SEQ ID NO:22 and 23 would provide information as to the presence of X or Y chromosomes.

Notwithstanding the amendments to the claims, claims 23 and 36, including claims depending thereform, never recited the terms at issue, thus, the rejection as applied to claims 23, 25, 26, 26, 38, 48, 80, and 81 is not appropriate.

Nevertheless, while Applicants do not acquiesce to the reasoning offered in the Action, and to expedite prosecution towards allowance, the amended claims no longer recite the terms at issue.

Regarding the statement that it is unclear as to how the non-consensus regions are used to detect the presence of X and Y chromosomes, the claims have been amended to clarify that detection is accomplished by amplification of non-consensus regions such that different length amplification products result if sequences comprising, for example, both SEQ ID NO:22 and SEQ ID NO:23, are present in the sample. Further, it is the detection of the presence or absence of such products which correlates with gender. Because the specification, including the Exhibits and Declaration previously presented, clearly show that detecting amplified products of different

lengths resulting from alignment gaps between the non-consensus sequences of the sequence identifiers recited clearly correlate with determination of gender, one of skill in the art would know the metes and bounds of the claims. That is all that is required.

For these reasons, Applicants respectfully request that the rejection be withdrawn.

Rejection Under 35 U.S.C. §112, First Paragraph

Claims 1, 3-9, 12, 13, 23, 25, 26, 36, 38, 48, 80, and 81 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking enablement.

Applicants traverse the rejection as it might apply to the amended claims, including claims dependent therefrom, for the reasons given below.

The Office Action alleges, in pertinent part, that the specification is not enabling because 1) the specification fails to make clear or provide any information or analysis regarding whether alleles are present on the opposite chromosome or whether the allele is present as an "uninformative SNP;" 2) it is not clear which polymorphisms are required to detect SEQ ID NO:23; 3) the teachings Tachi strongly indicate that polymorphisms of the nucleotides as well as the amino acid sequence might exist in a particular region of AMELX, depending upon the different breeds of domestic dogs; 4) it is unclear what the consensus sequence represents and because Figure 5 does not appear to show residues that are always conserved, it is not clear "which residues are variable with their variable sites;" and 5) the declaration provides no evidence that the detection using the specific primers to obtain a 140 or 142bp amplicon indicates that any non-consensus region or any difference is indicative of gender discrimination. Applicants respectfully submit that such allegations are misplaced.

Notwithstanding the amended claims, claims 23, 25, and 26 are not directed to determination of gender, therefore, the rejection as applied to these claims is not appropriate. Further, it is not clear what one of skill in the art would understand the Examiner's use of "alleles on opposite chromosomes" to mean with respect to X and Y chromosomes, since it is possible that a cell may contain an XX karyotype or XY karyotype, and it would not be clear which is considered opposite.

Nevertheless, regarding alleles, the arguments as presented in the Office Action continue to focus on SNPs. SNPs are defined as the occurrence of single base variations in the genetic code, these are limited to transitions and transversions.[1] With the exception of claims directed to microsatellite multiplex amplification (i.e., claims 36, 38, 48, 80, and 81), the methods as claimed do not detect SNPs. The methods exploit the gaps in the non-consensus sequences between SEQ ID NO:22 and SEQ ID NO:23. The primers required for amplification flank these specific regions, and because the gaps exist between the non-consensus sequences of the identifiers recited, amplicons are generated that have different lengths when sequences comprising both SEQ ID NO:22 and SEQ ID NO:23 are present in a sample. Further, because the specification provides methods for identifying non-consensus sequences, such as by hybridization, sequencing, and/or number/size differentiation of PCR products, including which non-consensus sequences are associated with each gender, sufficient guidance is provided to determine gender irrespective of whether the allele is present as an uninformative SNP.

Regarding which polymorphisms are required to detect SEQ ID NO:23, again the Action seems to focus on SNPs or polymorphisms that might or might not exist as illustrated by the shaded areas of Figure 5 (e.g., in the event that a dog contained a C at position 52, it is not clear whether this is informative). Again, this is not relevant to the method as claimed. The consensus sequences are the sequences which are outside of the shaded areas of the Figure. The informative sequences are the residues between the identifiers which are illustrated as gaps, not as transitions or transversions. Primers for amplification bind to consensus sequences that flank non-consensus sequences, which non-consensus sequences possess alignment gaps when the identifier residues are compared. Again, such gaps in alignment are exploited to produce amplicons which will vary in length when samples comprise sequences as set forth in both SEQ ID NO:22 and SEQ ID NO:23.

Regarding the teachings of Tachi, the Action fails to consider that the statement recited expressly limits the conclusion to a "particular region of AMELX." This region is not the same as the region recited in the instant specification. Further, Tachi only offers the possibility that

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[1] Oxford Dictionary of Biochemistry and Molecular Biology (Revised ed. 2001).

polymorphisms might exist in the region identified by the cited reference. Even this possibility must be met with suspicion, since it is based on unpublished results, as admitted by the author at page 635, col. 3, third paragraph.

Further, the position of the Action is not well supported given that the comparison in Figure 2 of Tachi does not compare alignments between an extinct Japanese wolf and a domestic dog, but in fact compares the sequence that is shared by the domestic dog and Mongolian wolf with a sequence of an extinct Japanese wolf. This would suggest that two separate species of canine (i.e., domestic dog and Mongolian wolf), not just breeds of dog, share 100% identity in this region (as admitted by Tachi at page 635, Col. 2, paragraph 2). As such, while Tachi might support the need for molecular analysis of the intraspecific as well as the interspecific variations of the AMELX DNA to examine an extinct Japanese wolf, the reference does not support such a position with respect to the domestic dog (or arguably the Mongolian wolf).

Regarding consensus, the Action states that the art suggests that the AMELX and AMELY genes are variable between species, and infers that differences that result from natural variation must be determined before gender differences can be discerned. It is unclear why this would be required. The specification clearly identifies the types of sequences which are embraced by the claims (e.g., paragraph [0016] and Table 3). Further, the inventors have demonstrated that in the absence of such information, gender was determined correctly in 100% of the samples tested (see, Item 3 in the **Declaration of Applicants Under 37 C.F.R §1.132**). Moreover, the method as claimed is robust and has a low error rate (see, Exhibit C of the **Declaration**).

Regarding the declaration and that any non-consensus region or any difference that is indicative of gender discrimination has not been provided, the claims as presently amended clearly recite the elements of the non-consensus region, such that any and all non-consensus regions are not embraced by the claims. Further, specific examples are provided showing the successful use of the probes/primers in the method as claimed (e.g., page 29, paragraph [0100] to page 31, paragraph [0105], and FIGS. 1-4, including that gender has been tested using these primers in over 10,000 dog samples from a wide range of breeds, and in all of these assays, gender was correctly identified: paragraph [0070]).

Regarding the Wands factors, 1) while the invention is in the biological arts, it is not necessary that every permutation within a generally operable invention be effective in order for an inventor to obtain a generic claim, provided that the effect is sufficiently demonstrated to characterize the generic invention. See, e.g., In re Angstadt, 537 F.2d 498, 504 (CCPA 1976). For the present set of facts, products associated with each gender were obtained as predicted from the disclosure, and such products were obtained consistently; 2) the number of successful applications of the method as recited in the specification (i.e., working examples) is **10,000**; 3) regarding guidance, one of skill in the art would recognize that the non-consensus regions are present only on the X or Y chromosome (all other chromosomes being excluded), thus, the ordinary artisan would be able to detect differences using this guidance; 4) regarding quantity of experimentation, such as design of appropriate consensus primers to flank non-consensus regions, development of conditions for hybridization or PCR, etc., these procedures are merely routine (e.g., see Example 1, at page 27, paragraph [0089] to page 31, paragraph [0107]), and do not rise to the level of undue experimentation; and 5) regarding the level of skill in the art (i.e., high), such a skilled artisan would have the knowledge and capabilities of using the information provided in the specification (i.e., design appropriate consensus primers to flank non-consensus sequences, develop conditions for hybridization or PCR, etc.) to make and use the invention commensurate in scope with the amended claims.

Therefore, the claims are enabled because the specification provides appropriate guidance, working examples, and prediction of success based on observed results using the claimed method such that one of ordinary skill in the art could practice the invention as claimed, in the absence of undue experimentation.

For these reasons, Applicants respectfully request that the rejection, including as it may be applied to the amended claims, be withdrawn.

Conclusion

Applicants submit that pending claims 1, 3-9, 12, 13, 23, 25, 26, 36, 38, 48, 80, and 81 are in condition for allowance. The Examiner is invited to contact Applicants' undersigned representative if there are any questions relating to this submission.

No fee is deemed necessary with the filing of this paper. However, the Commissioner is hereby authorized to charge any fees required by this submission, or credit any overpayments, to Deposit Account No. 07-1896 referencing the above-identified docket number. A duplicate copy the Transmittal Sheet is enclosed.

Respectfully submitted,

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